Remarks

Introduction

Claims 1-9, 17-25, and 28-33 remain pending.

Rejections Under 35 U.S.C. § 103

Claims 1-9, 17-25, and 28-33 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ludlow et al. in view of Simpson (1991) and further in view of Jankovic et al (1991).

The Office Action indicates that it would have been obvious to a person of ordinary skill in the art to administer botulinum toxin type F in combination with botulinum toxin type A because the patients had developed antibodies to toxin A (emphasis added; Office Action, page 4, second full paragraph and page 6, second full paragraph). The Office Action also indicates that it would have been obvious to a person of ordinary skill in the art to extend the teachings of Ludlow to serotypes other than type F, and to administer the other serotypes after A as claimed with a reasonable expectation of success (emphasis added; Office Action, page 4, second full paragraph and page 6, second full paragraph).

Applicant traverses the rejections.

Claim 1 is directed to a method that comprises a step of administering simultaneously to a patient a therapeutically effective amount of a combination of at least two neurotoxins.

Claim 17 is directed to a composition (e.g., one composition) that comprises a therapeutically effective amount of a combination of at least two neurotoxins. Claim 18 is directed to a therapeutic composition (e.g., one composition) that comprises botulinum toxin types A and B. Claim 29 is directed to a therapeutic composition (e.g., one composition) that comprises botulinum toxin types A and E. Claim 30 is directed to a therapeutic composition (e.g., one composition) that comprises at least two different types of botulinum toxin.

In short, the present claims are directed to methods that comprise simultaneously administering at least two types of botulinum toxin, and single compositions that comprise two or more types of botulinum toxin. In other words, the present claims are directed to subject matter that is different and distinct from methods which comprise administering non-type A serotypes of botulinum toxin after type A toxin has been administered to a patient, as stated in the Office Action.

Ludlow et al. discloses treatment of torticollis by administering botulinum toxin type F to patients who have antibodies to botulinum toxin type A. Ludlow discloses a composition which comprises only one type of botulinum toxin, i.e., botulinum toxin type F. Ludlow discloses a method of treating a patient by administering botulinum toxin type F to a patient at a different time (i.e., not simultaneously) than botulinum toxin type A, for example, botulinum toxin type F is administered to the patients after the patients received botulinum toxin type A therapy.

Simpson is a review article describing various features of botulinum toxin, including distinct antigenicities among the various serotypes and similar properties of inhibiting acetylcholine release. Although Simpson discloses that the different serotypes share a common feature of inhibiting acetylcholine release, Simpson also discloses that the mechanisms of action vary among the different serotypes.

Jankovic is a review article discussing therapeutic uses of botulinum toxin type A. Jankovic discloses that patients with antibodies against botulinum toxin type A will likely respond to injections with other botulinum toxins that are immunologically distinct from botulinum toxin type A.

Applicant submits that the combination of Ludlow, Simpson, and Jankovic does not disclose, teach, or suggest the present invention. For example, the combination of Ludlow, Simpson, and Jankovic does not disclose, teach, or even suggest a method which comprises simultaneous administration (e.g., at the same time, not at different times), or a single composition that comprises at least two different types of botulinum toxin.

Significantly, the Office Action acknowledges the deficient teachings of the combination of references. In particular, the Office Action specifically states that it would be obvious to administer a non-type A serotype of botulinum toxin after separate administration of botulinum toxin type A.

The characterization of the claimed invention in the Office Action is simply incorrect. The present claims are directed to a method which comprises simultaneously administering at least

two different types of botulinum toxin. In other words, the second botulinum toxin is not administered after the type A botulinum toxin is administered. In direct contrast, the prior art only teaches the sequential (i.e., not simultaneous) administration of a single type of botulinum toxin (type F) after administration of a botulinum toxin type A and the development of antibodies to type A botulinum toxin. The prior art does not disclose, teach, or even suggest administration of two or more botulinum toxins at the same time.

Thus, applicant submits that the combination of Ludlow et al., Simpson, and Jankovic does not disclose, teach, or even suggest all of the elements recited in the present claims.

It is well established that a proper rejection under 35 U.S.C. § 103 must be based on a showing of reasons that a person of ordinary skill in the art, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed." (*In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998)). Applicant submits that the cited references, taken alone or in any combination, do not disclose, teach, or even suggest administering two or more different botulinum toxins simultaneously, and do not disclose, teach, or even suggest two or more different types of botulinum toxin in a single composition. Thus, the rejections of the claims under 35 U.S.C. § 103 cannot be properly maintained and should be withdrawn.

In addition, applicant submits that the general disclosure by Simpson of the different serotypes of botulinum toxin does

not provide any motivation or incentive to a person of ordinary skill in the art to combine Ludlow et al., Simpson, and Jankovic for any purpose, let alone to combine Ludlow et al., Simpson, and Jankovic and specifically provide at least two different botulinum toxin types in a single composition, as recited in claims 17-25 and 28-33.

In specific reference to claims 28, 29, and 33, applicant submits that, based on the teachings of Ludlow et al., Simpson, and Jankovic, alone or in any combination, a person of ordinary skill in the art would still be required to guess, test, speculate, and/or arbitrarily "pick and choose" two specific neurotoxins (e.g., botulinum toxin types A and B or A and E) from among the list of seven different botulinum toxins identified by Simpson, as recited in claims 28-29. Simpson does not place any significance whatsoever in the types of botulinum toxin, let alone in a combination of botulinum toxin types A and B, or A and E, relative to the other botulinum toxins disclosed.

Simply put, the general disclosure in Simpson of botulinum toxin A through G is insufficient for Simpson, alone or in any combination with Ludlow et al. and Jankovic, to teach or suggest the compositions recited in claims 28, 29, and 33. For example, the general disclosure of botulinum toxin types A through G is insufficient for Simpson, alone, or in combination with Ludlow et al. and Jankovic, to teach or suggest a therapeutic composition comprising botulinum toxin types A and B or botulinum toxin types A and E, as recited in claims 28, 29, and 33.

Only after knowing of applicant's invention and disclosure would one of ordinary skill in the art select and combine two or more different types of botulinum toxin, such as types A and B, or A and E, in a single composition from among the seven different botulinum toxins disclosed by Simpson. Applicant submits that such hindsight is an improper basis for rejecting patent claims.

In addition, applicant submits that the prior art does not disclose, teach, or even suggest the composition of claim 30, wherein the amount of the first neurotoxin is greater than the amount of the second neurotoxin, as recited in claim 31. As discussed above, applicant submits that the prior art does not disclose, teach, or even suggest a single composition comprising two or more different botulinum neurotoxins, let alone, disclose, teach, or suggest the specific amounts of the botulinum neurotoxins, as recited in claims 30 and 31.

In view of the above, applicant submits that the present claims, and claims 1-9, 17-25 and 28-33 are unobvious from and patentable over Ludlow et al., Simpson, and Jankovic, alone or in any combination, under 35 U.S.C. § 103.

Each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art disclose, teach, or even suggest the present methods and compositions including the additional feature or features recited in any of the present dependent claims, such as the specific combinations of neurotoxins. Therefore, applicant submits that each of the present claims is separately patentable over the prior art.

Conclusion

In conclusion, applicant has shown that the present claims are unobvious from and patentable over the prior art under 35 U.S.C. § 103. Therefore, applicant submits that the present claims, that is claims 1-9, 17-25, and 28-33 are allowable. Therefore, applicant respectfully requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

Respectfully submitted,

Date: 6/13/05

Frank J. Uxa
Attorney for Applicant
Registration No. 25,612
4 Venture, Suite 300
Irvine, California 92618
(949) 450-1750
(949) 450-1764 Facsimile